REMARKS

Claims 1 to 33 are pending. Claims 21 to 33 have been withdrawn from consideration as directed to non-elected subject matter. Claims 1, 3, 7, 9, 12, 14, 17, 19 have been amended herein; claims 2, 8, 13, 18 and 21 to 33 have been canceled herein, and new claims 34 to 45 have been added herein. Therefore, upon entry of the amendment, claims 1, 3 to 7, 9 to 12, 14 to 17, 19, 20 and 34 to 45 will be under examination.

Regarding the Amendments

Claims 1, 7, 12, and 17 have been amended to recite an ADP-glucose receptor polypeptide containing SEQ ID NO:2, or a minor modification of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose. Support for the amendments to claims 1, 7, 12 and 17 can be found in the specification, for example, at page 6, line 28, to page 7, line 4, which indicates that the term "ADP-glucose receptor" refers to a polypeptide containing the amino acid sequence designated SEQ ID NO:2, or a polypeptide containing minor modifications of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose.

Claims 3, 9, 14, and 19 have been rewritten in independent form. Support for the amendments to claims 3, 9, 14 and 19 can be found, for example, in claims 1 and 3; claims 7 and 9; claims 12 and 14; and claims 17 and 19, respectively, as originally filed.

New claims 34 to 45 are directed to methods of identifying an ADP-glucose receptor agonist, antagonist or ligand using an ADP-glucose receptor polypeptide that has at least 85% identity to SEQ ID NO:2 (claims 34, 37, 40 and 43); at least 95% identity to SEQ ID NO:2 (claims 35, 38, 41 and 44); or at least 99% identity with SEQ ID NO:2 (claims 36, 39, 42 and 45). Support for new claims 34 to 45 can be found in the specification, for example, at page 16, lines 20-24, which indicates that an ADP-glucose receptor polypeptide can have at least 80%, 85%, 90%, 95%, 98%, 99% or greater identity to SEQ ID NO:2.

Attached hereto as Appendix 1 is a marked up version of the amendments, in which added text is underlined and deleted text is enclosed in brackets.

Regarding the Drawings

The Office Action states that Figures 2 through 5 are objected to as being allegedly illegible. Applicants submit herewith new copies of Figures 2 through 5 for the Examiner's use. Formal drawings will be filed upon allowance of the subject application.

Regarding the Information Disclosure Statement

The Office Action states that the Information Disclosure Statement filed on August 12, 2002, is incomplete for

lacking dates corresponding to GenBank citations. Applicants submit herewith a new PTO Form 1449 as Exhibit G, which has been updated to include a publication date for each GenBank citation. Applicants point out that the listed dates are identical to those shown on corresponding GenBank database print-outs that were originally filed with the Information Disclosure Statement.

Regarding the Claim Objections

The Office Action states that claims 3, 9, 14 and 19 are objected to as each depending upon a rejected base claim. Applicants have herein amended claims 3, 9, 14 and 19 to independent form. Therefore, these claims are in condition for allowance.

Regarding the rejection under 35 U.S.C. § 112, first paragraph

The objection to the specification and corresponding rejection of claims 2, 8, 13 and 18 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement are respectfully traversed.

The Office Action acknowledges that the specification is enabling for methods of identifying a ligand, agonist or antagonist of an ADP-glucose receptor having SEQ ID NO:2. However, the Office Action alleges that the specification lacks enablement for methods of identifying a ligand, agonist or antagonist of the ADP-glucose receptor having a sequence with at least 70% identity to SEQ ID NO:2.

In particular, the Office Action alleges that the specification lacks sufficient description of the structural and functional features of an ADP-glucose receptor to enable methods that employ an ADP-glucose receptor having a sequence with at least 70% identity with SEQ ID NO:2. Specifically, the Office Action states that the specification lacks guidance regarding (i) which modifications can be made to SEQ ID NO:2 that will result in a protein having the same function as SEQ ID NO:2, and (ii) which portions of SEQ ID NO:2 are critical for binding or functional activity of the receptor.

Regarding which modifications can be made to SEQ ID NO:2 that will result in a protein having the same function as SEQ ID NO:2, Applicants respectfully submit that the specification provides guidance that would have allowed one skilled in the art to obtain a variety of minor modifications of SEQ ID NO:2 that transduce a G-protein coupled signal in response to ADP-glucose without undue experimentation. In particular, it would have been within the ability of one skilled in the art to obtain a naturally occurring modification of SEQ ID NO:2, such as an ortholog, splice variant or polymorphism-derived modification of SEQ ID NO:2, using routine cloning methods.

As evidence that modifications of ADP-glucose receptor SEQ ID NO:2 would have been routinely obtained, Applicants submit Exhibits A through C, which show nucleotide and amino acid sequences of orthologs of SEQ ID NO:2 identified in several species after the priority date of the subject application. Exhibit A shows that a rat ortholog of SEQ ID NO:2 was reported

on January 12, 2001; Exhibit B shows that a macaque ortholog of SEQ ID NO:2 was reported on March 1, 2001; and Exhibit C shows that a mouse ortholog of SEQ ID NO:2 was reported on December 5, 2002. Applicants also submit Exhibits D through F, which show alignments of SEQ ID NO:2 with the reported rat, mouse and macaque orthologs, respectively. The alignments show that SEQ ID NO:2 and the corresponding orthologs are highly related, each ortholog having between 86-97% identity with SEQ ID NO:2 across the compared amino acids.

Using guidance provided in the specification, including nucleotide and amino acid sequences of human ADP-glucose receptor (SEQ ID NOS:1 and 2, respectively), a variety of orthologs of SEQ ID NO:2 would have by obtained by one skilled in the art. Functional activity of such modifications of SEQ ID NO:2 would have been tested using methods provided in the specification, and active modifications used in the claimed methods of identifying ADP-glucose receptor ligands, agonists and antagonists. With regard to methods for obtaining such naturally occurring modifications of SEQ ID NO:2, the specification describes library screening with a detectable ADP-glucose receptor nucleic acid molecule or antibody to identify an ADP-glucose receptor nucleic acid molecule. The specification also describes PCR amplification of a nucleic acid molecule encoding an ADP-glucose receptor (page 26, line 20, to page 27, line 3). In view of these teachings in the specification, one skilled in the art would have been able to use a variety of routine molecule biology procedures to obtain a minor modification of SEQ ID NO:2 that retains function.

Further regarding which modifications can be made to SEQ ID NO:2 that will result in a protein having the same function as SEQ ID NO:2, Applicants respectfully submit that the specification teaches several approaches for determining amino acid residues that can be modified without abolishing the function of a polypeptide. Such approaches would have been used by one skilled in the art to obtain a variety of non-naturally occurring modifications of SEQ ID NO:2 that retain function. For example, the specification teaches that a computer program, such as that described in Eroshkin et al., (page 10, lines 10-14); and that structure function studies of other G-protein coupled receptors, such as those described in Flower et al. and Wess et al. (page 10, line 15, to page 11, line 7), are useful for predicting modifications of SEQ ID NO:2 that have the same function as SEQ ID NO:2. Moreover, the specification teaches several conservative amino acid substitutions, such as substitution of an apolar amino acid with another apolar amino acid (page 11, line 25, to page 12, line 12) that would have been made by one skilled in the art to obtain a modification of SEQ ID NO:2 that retains function. Using this guidance, one skilled in the art would have been able to determine which modifications can be made to SEQ ID NO:2 to obtain a protein that retains the function of SEQ ID NO:2.

The specification also provides guidance for preparing an ADP-glucose receptor, such as a naturally occurring or non-naturally occurring of SEQ ID NO:2, and guidance for confirming that an ADP-glucose receptor has functional activity. In particular, the specification teaches that an ADP-glucose

receptor polypeptide can be prepared using recombinant methods and biochemical procedures (page 31, line 6, to page 32, line 14). The specification also teaches that an ADP-glucose receptor polypeptide can be tested for functional activity using a variety of assays, including receptor signaling assays and physiological assays. A receptor signaling assay is exemplified in the specification, for example, at page 61, lines 11-30; and page 62, lines 14-25, which describes calcium mobilization assays in which ADP-glucose receptor signaling in response to ADP-glucose induced a transient increase in intracellular calcium in CHO cells. Physiological assays are exemplified in the specification, for example, in Figures 5A, 5B and 5C, which show ADP-glucose-induced inhibition of spontaneous, electrically-evoked, or histamine induced contractions of ileal tissue, respectively, and in Figures 6A and 6B, which show ADP-glucose-induced inhibition of phenylephrine-evoked and serotonin-evoked contractions of arterial tissue, respectively (page 35, line 16, to page 36, line 4). In view of this guidance in the specification, Applicants submit that one skilled in the art would have been able to prepare a modification of SEQ ID NO:2 and determine that the polypeptide had the same function as SEQ ID NO:2 without undue experimentation.

Regarding the portions of SEQ ID NO:2 that are critical for binding or functional activity of ADP-glucose receptor, Applicants respectfully submit that this information is unimportant with respect to naturally occurring modifications of SEQ ID NO:2, such as species orthologs of SEQ ID NO:2, which, as described above, would have been identified by one skilled in the

art using routine methods. With respect to non-naturally occurring modifications of SEQ ID NO:2, the specification teaches that once orthologs of SEQ ID NO:2 from other species are identified, the sequences can be compared with SEQ ID NO:2 to determine which portions of SEQ ID NO:2 can be modified while retaining functional activity of the receptor (page 11, lines 23-24). Further, the specification teaches additional approaches for determining amino acid residues that can be modified without abolishing the function of a polypeptide, as described above.

In view of the above, Applicants respectfully submit that the specification provides sufficient guidance to enable methods for identifying an ADP-glucose receptor ligand, agonist or antagonist that employ minor modifications of SEQ ID NO:2, such as species orthologs and other highly related ADP-glucose receptors capable of transducing a G-protein coupled signal in response to ADP-glucose. Nevertheless, claims 2, 8, 13 and 18 have been canceled herein to advance prosecution of this application. Thus, the rejection of claims 2, 8, 13 and 18 under 35 U.S.C. § 112, first paragraph, is rendered moot.

Applicants point out that new claims 34 to 45 are directed to methods of identifying an ADP-glucose receptor agonist, antagonist or ligand using an ADP-glucose receptor polypeptide that has at least 85% identity to SEQ ID NO:2 (claims 34, 37, 40 and 43); at least 95% identity to SEQ ID NO:2 (claims 35, 38, 41 and 44); or at least 99% identity with SEQ ID NO:2 (claims 36, 39, 42 and 45). As described above, such minor modifications of SEQ ID NO:2 would have been obtained by one

skilled in the art without undue experimentation. Therefore, Applicants believe that claims 34 to 45 are enabled by the specification.

Regarding the rejection under 35 U.S.C. § 102

The rejection of claims 1, 4 to 7, 10 to 12, 15 to 17 and 20 under 35 U.S.C. § 102, as allegedly anticipated by WO 99/57245 is respectfully traversed.

The Office Action alleges that WO 99/57245 describes a method for identifying an agonist, antagonist or ligand of the KIAA0001 polypeptide, which is a G-protein coupled receptor for UDP-glucose, in the presence of ADP glucose.

Independent claims 1, 7, 12 and 17 are directed to methods of identifying either an ADP-glucose receptor agonist or antagonist (claims 1 and 12), or an ADP-glucose receptor ligand (claims 7 and 17). These methods involve contacting an ADP-glucose receptor with one or more candidate compounds under conditions in which the receptor produces a G-protein coupled signal in response to ADP-glucose (claims 1 and 12) or selectively binds to ADP-glucose (claims 7 and 17). In contrast, WO 99/57245 describes methods of identifying agonists and antagonists of a UDP-sugar receptor (KIAA0001). The UDP-sugar receptor described in WO 99/57245 is functionally distinct from the ADP-glucose receptor recited in the claimed methods. Whereas the specification teaches that an ADP-glucose receptor has an ability to transduce a G-protein coupled signal in response to

ADP-glucose, WO 99/57245 exemplifies that KIA0001 failed to transduce a G-protein coupled signal in response to ADP-glucose (see Example 8, page 27, lines 26-31). Therefore, WO 99/57245 does not teach the ADP-glucose receptor recited in the claimed methods.

Moreover, as amended, independent claims 1, 7, 12 and 17 recite an ADP-glucose receptor polypeptide that contains SEQ ID NO:2, or a minor modification of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose. In contrast, the UDP-sugar receptor described in WO 99/57245 is unrelated to SEQ ID NO:2, having only 43% overall amino acid identity with SEQ ID NO:2 (page 6, point 9 of the Office Action mailed September 24, 2002). Thus, the UDP-sugar receptor described in WO 99/57245 is structurally distinct from the ADP-glucose receptor recited in the claimed methods. In the absence of a teaching of the structural characteristics of the ADP-glucose receptor recited in the claimed methods, WO 99/57245 cannot anticipate claims 1, 7, 12 or 17.

For these reasons, claims 1, 4 to 7, 10 to 12, 15 to 17 and 20, which recite an ADP-glucose receptor having functional and structural characteristics distinct from the UDP-sugar receptor described in WO 99/57245, cannot be anticipated by WO 99/57245. Accordingly, Applicants respectfully request removal of the rejection of claims 1, 4 to 7, 10 to 12, 15 to 17 and 20 under 35 U.S.C. § 102, as allegedly anticipated by WO 99/57245

CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney or Cathryn Campbell.

Respectfully submitted,

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APPENDIX 1

1. (Amended) A method of identifying an ADP-glucose receptor agonist or antagonist, comprising:

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds under conditions wherein said receptor produces a G-protein coupled signal in response to ADP-glucose**, wherein said ADP-glucose receptor polypeptide comprises SEQ ID NO:2, or a minor modification of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose**; and

(b) identifying a candidate compound that alters production of said signal, said compound being characterized as a ADP-receptor agonist or antagonist.

3. (Amended) **[The method of claim 1,] A method of identifying an ADP-glucose receptor agonist or antagonist, comprising:**

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds under conditions wherein said receptor produces a G-protein coupled signal in response to ADP-glucose, wherein said ADP-glucose receptor polypeptide has the amino acid sequence designated SEQ ID NO:2**; and**

(b) identifying a candidate compound that alters production of said signal, said compound being characterized as a ADP-receptor agonist or antagonist.

7. (Amended) A method of identifying an ADP-glucose receptor ligand, comprising:

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds under conditions wherein said receptor selectively binds ADP-glucose**, wherein said ADP-glucose receptor polypeptide comprises SEQ ID NO:2, or a minor modification of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose**; and

(b) identifying a candidate compound that selectively binds said ADP-glucose receptor polypeptide, said compound being characterized as an ADP-receptor ligand.

9. **[The method of claim 7,] A method of identifying an ADP-glucose receptor ligand, comprising:**

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds under conditions wherein said receptor selectively binds ADP-glucose, wherein said ADP-glucose receptor polypeptide has the amino acid sequence designated SEQ ID NO:2**; and**

(b) identifying a candidate compound that selectively binds said ADP-glucose receptor polypeptide, said compound being characterized as an ADP-receptor ligand.

12. (Amended) A method of identifying an ADP-glucose receptor agonist or antagonist, comprising:

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds in the presence of ADP-glucose under conditions wherein said receptor produces a

G-protein coupled signal in response to ADP-glucose**, wherein said ADP-glucose receptor polypeptide comprises SEQ ID NO:2, or a minor modification of SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose**; and

(b) identifying a candidate compound that alters production of said signal, said compound being characterized as a ADP-receptor agonist or antagonist.

14. (Amended) **[The method of claim 12,] A method of identifying an ADP-glucose receptor agonist or antagonist, comprising:**

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds in the presence of ADP-glucose under conditions wherein said receptor produces a G-protein coupled signal in response to ADP-glucose, wherein said ADP-glucose receptor polypeptide has the amino acid sequence designated SEQ ID NO:2**; and**

(b) identifying a candidate compound that alters production of said signal, said compound being characterized as a ADP-receptor agonist or antagonist.

17. (Amended) A method of identifying an ADP-glucose receptor ligand, comprising:

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds in the presence of ADP glucose under conditions wherein said receptor selectively binds ADP-glucose**, wherein said ADP-glucose receptor polypeptide comprises SEQ ID NO:2, or a minor modification of SEQ ID NO:2**

that transduces a G-protein coupled signal in response to ADP-glucose; and

(b) identifying a candidate compound that selectively binds said ADP-glucose receptor polypeptide, said compound being characterized as an ADP-receptor ligand.

19. (Amended) **[The method of claim 17,] A method of identifying an ADP-glucose receptor ligand, comprising:**

(a) contacting an ADP-glucose receptor polypeptide with one or more candidate compounds in the presence of ADP glucose under conditions wherein said receptor selectively binds ADP-glucose, wherein said ADP-glucose receptor polypeptide has the amino acid sequence designated SEQ ID NO:2**; and**

(b) identifying a candidate compound that selectively binds said ADP-glucose receptor polypeptide, said compound being characterized as an ADP-receptor ligand.